

# SIDE-EFFECTS OF TOBACCO & ALCOHOL IN EARLY PREGNANCY



**ERIC JAUNIAUX**  
 Institute for Women's Health  
 @ University College London

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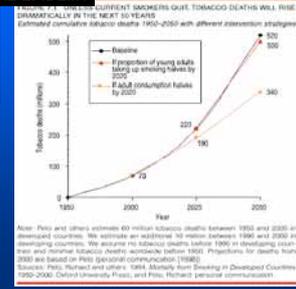
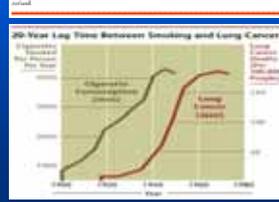
# TOBACCO: EPIDEMIOLOGY



## THE GLOBAL EPIDEMY

**TABLE 2.1 CURRENT AND ESTIMATED FUTURE DEATHS FROM TOBACCO (millions per year)**

	Number of tobacco deaths in 2000	Number of tobacco deaths projected for 2025
Developed	2	3
Developing	2	3




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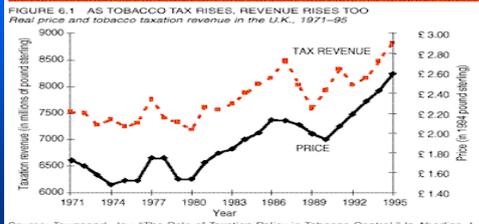
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# TOBACCO: EPIDEMIOLOGY



Source: Townsend, Joy, "The Role of Taxation Policy in Tobacco Control." In Abernethy, J., and others, eds. *The Economics of Tobacco Control*. Cape Town, South Africa: Applied Fiscal Research Centre, University of Cape Town.

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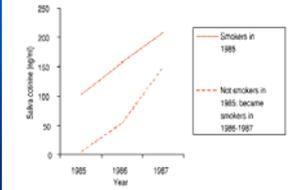
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# TOBACCO: EPIDEMIOLOGY



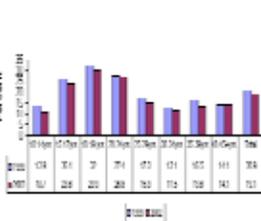
## IMPACT OF AGE: TEEN DISEASE

FIGURE 2.1 NICOTINE INTAKE LEVELS CLIMB RAPIDLY IN YOUNG SMOKERS  
Saliva concentrations of cotinine in a group of adolescent girls in the United Kingdom



Source: McNeill, A. D. and others, 1989. "Nicotine Intake in Young Smokers: Longitudinal Study of Saliva Cotinine Concentrations." *American Journal of Public Health* 79(2): 172-75.

Maternal Smoking by Age of Mother: Indiana, 1989 and 2002




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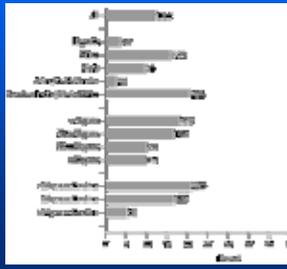
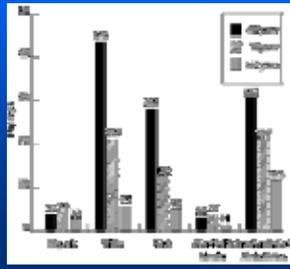
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# TOBACCO: EPIDEMIOLOGY



## IMPACT OF EDUCATION: SOCIAL DISEASE




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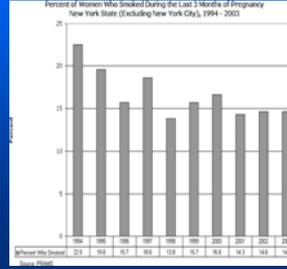
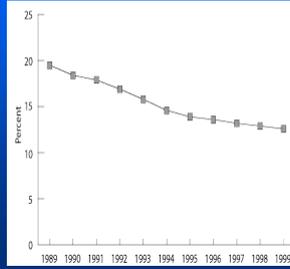
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# TOBACCO: EPIDEMIOLOGY



## IMPACT OF ADVERTISING: MEDIA




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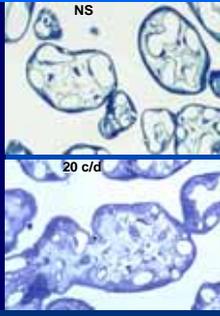
## Placental morphological and biological changes associated with maternal smoking

### Increased

- Trophoblastic and villous membrane thickness.
- Syncytiotrophoblastic necrosis.
- Thickness of the trophoblast basal membrane.
- Apoptosis in the syncytiotrophoblast.
- Expression of pVHL, HIFs, and VEGFs.
- Stimulation of nicotinic acetylcholine receptors.
- Level of metallothionein.
- Vasoconstrictive response to endothelin 1

### Decreased

- Decrease in villous capillary volume fraction.
- Decrease in total surfaces of syncytial knots.
- Synthesis and activation of the 92 kDa type IV collagenase.
- Cytotrophoblast expression of I-selectin and TRA-1-81-reactive carbohydrate ligands.
- Expression and activity of 11 beta-hydroxysteroid dehydrogenase type 2.
- Progesterone synthesis.
- Enzymatic activity of complex III and mitochondrial DNA.




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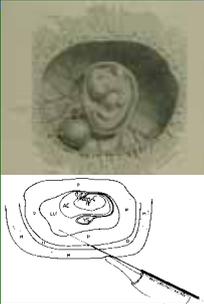
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## EARLY TRANSFER OF TOBACCO-DERIVED MOLECULES

### • COELO & CORDOCENTESIS

- Cotinine is found inside the GS from 6 wks.
- Cotinine level in CF > MS
- Cotinine level @ 11-17 wks in FS > MS
- FP levels of Ser, Pro,  $\alpha$ -amino-butyric ac, Leu & Arg are lower @12-17 wks in Smokers.




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## CIGARETTE SMOKING AND OFR

- # Smoking is associated with increased blood levels of glutathione (GSSP) (Muscat et al. FR Biol Med 2004).
- # Cigarette smoke extract decreases iNOS expression and NO production (Hoyt et al. Exp Lung Res. 2003).
- # Smokers have significantly lower plasma ascorbic acid (Dieterich et al., AJ Clin Nut. 2003).
- # Activities of SOD and CAT in erythrocytes are significantly lower in active and passive smokers (Yildiz et al., Clin Chem Lab Med. 2002).



TOBACCO SMOKE INDUCES **DIRECT DAMAGES** (CADMIUM) AND **INDIRECT DAMAGES** VIA AN INCREASE INTAKE OF FREE RADICAL AND DECREASE ANTIOXYDANT ENZYME ACTIVITY

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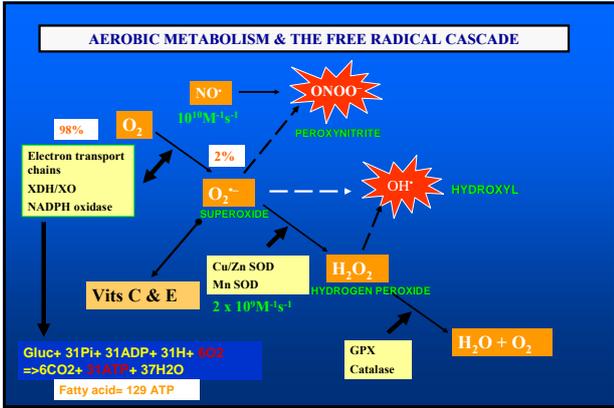
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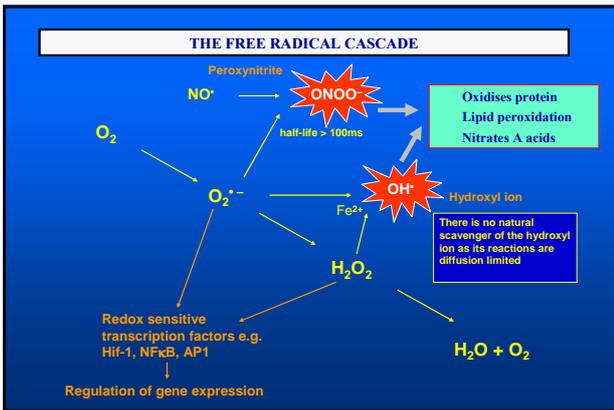
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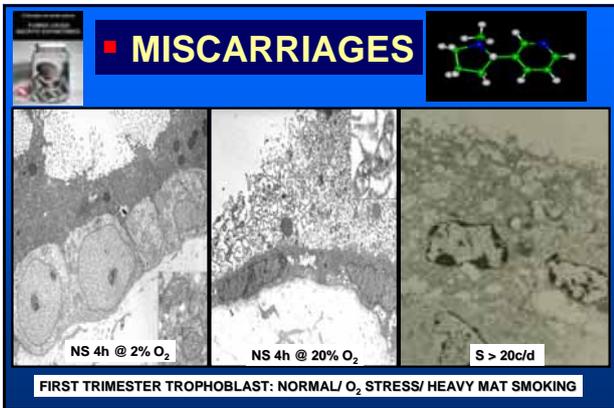
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**Placental and fetal side-effects of maternal tobacco smoking in early pregnancy**

- Miscarriage
- Ectopic pregnancy
- Placenta previa & placenta previa-accreta
- Fetal orofacial clefts




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**OROFACIAL CLEFTS**

Among fetuses lacking enzymes involved in the detoxification of tobacco-derived chemicals (Lammer et al., Epidemiology, 2004 & 2005)




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**Maternal smoking & placenta previa**

Sathu et al., EHD, 2007



Reference	Outcome	Study Design	Site, Sample Size	Findings
Meyer et al 1976	Placenta Previa	Retrospective Cohort	Canada 51,490 births	RR <sup>2</sup> = 1.43
Williams et al 1991	Placenta Previa	Case-Control	United States 69 cases/12,351 controls	OR <sup>2</sup> = 2.6 (95% CI: 1.3 - 5.5)
Monica & Lilja 1995	Placenta Previa	Case-Control	Sweden 3278 cases/3270 controls	OR = 1.53 (95% CI: 1.40-1.67)
Ananth et al 1996	Placenta Previa	Retrospective Cohort	Canada 61,667 women	OR = 1.36 (95% CI: 1.04 - 1.79)

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## Placental and fetal side-effects of maternal tobacco smoking in early and late pregnancy



- Fetal growth restriction
- Placental insufficiency
- Placental abruption
- PROM
- Preterm delivery
- IUD




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## Maternal smoking & placenta abruptio



Salihu et al., EHD, 2007

Reference	Outcome	Study Design	Site, Sample Size	Findings
Voigt et al 1990	Abruptio Placentae	Case-Control	United States 1406 cases/2874 controls	OR = 1.6 (95% CI: 1.3 - 1.8)
Castles et al 1999	Abruptio Placenta	Case-Control	United States 37 cases/51 controls	OR = 4.0 (95% CI: 1.5 - 11.0)
Ananth et al 2001	Placental Abruption	Retrospective Cohort	United States 7,465,858 singleton births	OR = 2.00 (95% CI: 1.95 - 2.05)

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## Maternal smoking & odds ratios for stillbirth in a case-control and case-crossover study



	Case-control OR (95% Confidence interval)	Bi-directional Case-crossover OR (95% Confidence interval)
Overall	1.34(1.26-1.43)	1.20 (1.03-1.39)
Number of c/day		
1-9	0.94(0.76-1.70)	1.16 (0.88-1.53)
10-19	1.31(1.22-1.41)	1.10 (0.90-1.24)
20 and above	1.43(1.31-1.57)	1.21 (1.01-1.50)

Salihu et al., EHD, 2007

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Indices of adverse birth outcomes among infants born to smoking mothers.

Indices	Magnitude of Association	Absolute Risk	Number Needed to Quit to prevent 1 AQ
Preterm	OR = 1.3 (95% CI 1.2-1.3)	4.8	21
Very Preterm	OR = 1.4 (95% CI 1.2-1.5)	1.4	71
SGA	OR = 2.3 (95% CI 2.2-2.4)	11.2	9
Infant Mortality	OR = 1.40 (95% CI 1.32-1.48)	0.4	250
Sudden Infant Death Syndrome	OR = 2.3 (95% CI 1.8-2.9)	0.16	625

Salihu et al., EHD, 2007

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**■ MATERNAL SMOKING IS THE MOST IMPORTANT MODIFIABLE PREGNANCY RISK FACTORS ASSOCIATED WITH ADVERSE PERINATAL OUTCOME.**




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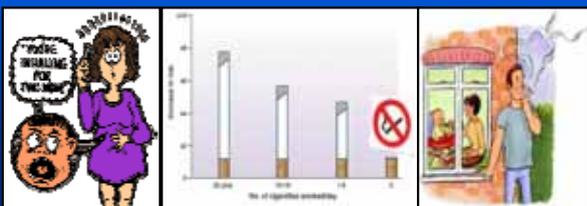
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- SMOKING DURING PREGNANCY (US):**
- Costs 250 millions \$/ year.
  - Additional 1500\$ to pregnancy costs.
  - A drop of 1% in maternal smoking prevalence prevents the delivery of 1300 LBW infants.




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## LONG TERM IMPACT OF MATERNAL SMOKING

- Has been associated with:

- Activation of nicotine Rec (12 wks) => Addiction in utero.
- Abnormal brain cell proliferation & differentiation => Cognitive deficits & attention deficit/hyperactivity disorder .
- Chromosome instability in amniocytes & blood SC => Childhood cancer.



+ Respiratory disorders & SIDS??

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## FETAL ALCOHOL SYNDROME (FAS)

- Low birth weight (Small head circumference).

- **Facial abnormalities:**

- \* Small upper jaw
- \* Short, upturned nose
- \* Smooth groove in upper lip
- \* Smooth and thin upper lip
- \* Narrow, small eyes with large **epicanthal folds**




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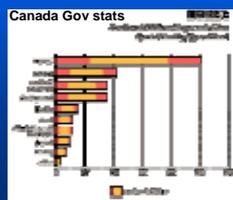
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## FAS: LONG TERM EFFECTS

- Has been associated with:

- Poor coordination/fine motor skills
- Poor socialization skills, such as difficulty building and maintaining friendships and relating to groups.
- Lack of imagination or curiosity
- Learning difficulties, including poor memory, inability to understand concepts such as time and money, poor language comprehension, poor problem-solving skills
- Behavioral problems, including hyperactivity, inability to concentrate, social withdrawal, stubbornness, impulsiveness, and anxiety




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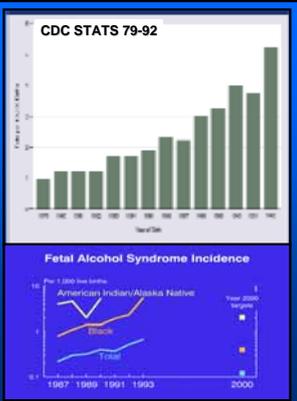
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## FAS: EPIDEMIOLOGY

- There is little research published on the prevalence, natural history, medical, and social complications relevant to adults with FAS.
- The evidence that is emerging suggests that this disorder is common, and that services to diagnose and treat these individuals are limited.




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## SMOKING vs ALCOHOL

### SMOKING AND PREGNANCY/FETUS

GOOGLE Hits: 9,800,000 + 2,010,000

=> 12 M

PUB-MED Hits: 9798 + 1295 => 11093

### ALCOHOL AND PREGNANCY/FETUS

GOOGLE Hits: 3,260,000 + 2,190,000

=> 5.4 M

PUB-MED Hits: 19254 + 4196 => 23450




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## ▪ FAS FACTS, POLITICS & THE MEDIA.




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## RM & PREVENTIVE MEASURES

ESHRE guidelines 2006

### • RISK FACTORS

- Stop Smoking (+ passive).
- Toxics (Caffeine, Alcohol, Radiations, Chemicals).
- Stable maternal health (BMI/Obesity)
- TLC (Stress).



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Thank You

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